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		<i>DB=USPT,EPAB,JPAB,DWPI,TDBD; PLUR=YES; OP=OR</i>	
<input type="checkbox"/>	L5	424/450.ccls. and (acrylic adj1 acid)	121
<input type="checkbox"/>	L4	L3 and 424/450.ccls.	21
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<input type="checkbox"/>	L2	(polyanionic) same (acrylic adj1 acid)	0
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L1: Entry 4 of 23

File: USPT

Aug 20, 2002

DOCUMENT-IDENTIFIER: US 6436905 B1

TITLE: Lipid-containing compositions and uses thereof

Brief Summary Text (18):

An example of one lipid-solubilizing synthetic amphipathic polymer including both hydrophobic groups and anionic hydrophilic groups which can be used in carrying out the invention is the homopolymer poly(2-ethyl acrylic acid) (PEAA) that has previously been reported as interacting in aqueous solutions at pH >7 with phosphatidylcholines such as dilauroylphosphatidylcholine (DLPC) and dipalmitoylphosphatidylcholine (DPPC) to yield suspensions of multilamellar vesicles which clear when the pH is lowered below a critical value of approximately 6.5. See for example K. Seki et al. (1984) "pH-Dependent Complexation of Poly (acrylic acid) Derivatives with Phospholipid Vesicle Membranes", *Macromolecules*, 17, 1692-1698, D. A. Tirrell et al. (1985) "pH Sensitisation of Phospholipid Vesicles via Complexation with Synthetic Poly(carboxylic acid)s", *Ann. N.Y. Acad. Sci* 446, 237-248, and K. A. Borden et al. (1987) "Polyelectrolyte adsorption induces a vesicle-to-micelle transition in aqueous dispersions of dipalmitoylphosphatidylcholine", *Polymer Preprints*, 28, 284-285).

Brief Summary Text (23):

In carrying out the invention, instead of PEAA other similar vinyl homopolymers of an acrylic acid derivative having a hydrophobic side chain, e.g. 2-propyl acrylic acid, or other poly(carboxylic acid) polymers having pendant hydrophobic side groups in addition to anionic hydrophilic groups, may be used. In preferred embodiments, however, the selected synthetic lipid-solubilizing amphipathic polymer will be a linear alternating vinyl copolymer formed by free radical addition polymerisation of an unsaturated dicarboxylic acid, or an anhydride or monoester of said dicarboxylic acid, with a monoenoic vinyl monomer or monomers in alternating relationship.

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L1: Entry 5 of 23

File: USPT

Jul 30, 2002

US-PAT-NO: 6426086

DOCUMENT-IDENTIFIER: US 6426086 B1

TITLE: pH-sensitive, serum-stable liposomes

DATE-ISSUED: July 30, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Papahadjopoulos; Demetrios	late of San Francisco	CA		
Meyer; Olivier	Strasbourg			FR
Leroux; Jean-Christophe	Montreal			CA

ASSIGNEE-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY	TYPE	CODE
The Regents of the University of California	Oakland	CA				02

APPL-NO: 09/ 243098 [\[PALM\]](#)

DATE FILED: February 2, 1999

PARENT-CASE:

CROSS-REFERENCES TO RELATED APPLICATIONS This case claims priority from U.S. Serial No. 60/073,471, filed Feb. 3, 1998, the contents of which are incorporated by reference.

INT-CL: [07] [A61](#) [K](#) [9/127](#)

US-CL-ISSUED: 424/450; 424/1.21, 424/9.321, 424/9.51, 424/94.3, 428/402.2, 935/54

US-CL-CURRENT: [424/450](#); [424/1.21](#), [424/9.321](#), [424/9.51](#), [424/94.3](#), [428/402.2](#)

FIELD-OF-SEARCH: 424/450, 424/1.21, 424/9.321, 424/9.51, 424/417, 424/94.3, 424/812, 436/829, 935/54, 428/402.2

PRIOR-ART-DISCLOSED:

U.S. PATENT DOCUMENTS

[Search Selected](#)[Search ALL](#)[Clear](#)

	PAT-NO	ISSUE-DATE	PATENTEE-NAME	US-CL
<input type="checkbox"/>	4448765	May 1984	Ash	424/450
<input type="checkbox"/>	5891468	April 1999	Martin	424/450

OTHER PUBLICATIONS

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- Brazel et al., "Pulsatile Local Delivery of Thrombolytic and Antithrombotic Agents Using Poly(N-isopropylacrylamide-co-methacrylic acid) Hydrogels," *J. Controlled Release*, 39:57-64 (1996).
- Chen et al., "Graft Copolymers that Exhibit Temperature-induced Phase Transitions Over a Wide Range of pH," *Nature*, 373:49-52 (1995).
- Collins et al., "Structural and Functional Comparisons of pH-Sensitive Liposomes composed of Phosphatidylethanolamine and Three Different Diacylsuccinylglycerols," *Biochimica et Biophysica Acta*, 1025:234-242 (1990).
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- Ellens et al., "pH-Induced Destabilization of Phosphatidylethanolamine-Containing Liposomes: Role of Bilayer Contact," *Biochemistry*, 23:1532-1538 (1984).
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- Kim et al., "Temperature-Sensitivity of Liposomal Lipid Bilayers Mixed with Poly(N-Isopropylacrylamide-co-acrylic Acid)," *J. Biochem.*, 121:15-19 (1997).
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- Kim et al., "Temperature-Sensitive Releases From Liposomes Containing Hydrophobically Modified Poly(N-Isopropylacrylamide)," *Korean J. Chem. Eng.*, 16:28-33 (1999).
- Kirpotin et al., "Liposomes with Detachable Polymer Coating: Destabilization and Fusion of Dioleoylphosphatidylethanolamine Vesicles Triggered by Cleavage of Surface-Grafted Poly(Ethylen Glycol)," *FEBS Letters*, 388:115-118 (1996).
- Kono et al., "Novel pH-Sensitive Liposomes: Liposomes Bearing a Poly(Ethylen Glycol) Derivative with Carboxyl Group," *Biochimica et Biophysica Acta*, 1193:1-9 (1994).
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- Litzinger et al., "Phosphatidylethanolamine Liposomes: Drug Delivery, Gene Transfer and Immunodiagnostic Applications," *Biochimica et Biophysica Acta*, 1113:201-227 (1992).

Liu et al., "Small, but Not Large, Unilamellar Liposomes Composed of Dioleoylphosphatidylethanolamine and Oleic Acid Can Be Stabilized by Human Plasma," *Biochemistry*, 28:7700-7707 (1989).

Liu et al., "pH-Sensitive Plasma-Stable Liposomes with Relatively Prolonged Residence in Circulation," *Biochimica et Biophysica Acta*, 1022:348-354 (1990).

Murthy, N., et al. "Design of Polymer to Increase the Efficiency of Endosomal Release of Drugs," *Proc. Intern. Symp. Control Rel. Bioact. Mater.*, 25:224-225 (1998).

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Wu et al., "Conjugation of Phosphatidylethanolamine to Poly(N-Isopropylacrylamide) for Potential Use in Liposomal Drug Delivery Systems," *Polymer*, 33:4659-4662 (1992).

ART-UNIT: 1615

PRIMARY-EXAMINER: Kishore; Gollamudi S.

ATTY-AGENT-FIRM: Townsend and Townsend and Crew, LLP

ABSTRACT:

This invention relates to the field of liposomes. In particular, this invention provides novel liposomes that are pH-sensitive, yet are also stable in serum. The liposomes are complexed with a molecule comprising a thermally-sensitive polymer showing lower critical solution temperature behavior in aqueous solutions, said thermally-sensitive polymer bearing a hydrophobic substituent and a pH sensitive substituent, wherein said hydrophobic substituent is less than 10 kD and which pH sensitive substituent remains ionizable following said covalent bonding to said thermally-sensitive polymer, and whose pH sensitive does not depend on cleavage of the covalent bond to said thermally-sensitive polymer. The invention further

relates to methods of conferring pH sensitivity upon liposomes by complexing the liposomes with such molecules.

33 Claims, 3 Drawing figures

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L1: Entry 17 of 23

File: USPT

May 1, 1990

DOCUMENT-IDENTIFIER: US 4921757 A

**** See image for Certificate of Correction ****

TITLE: System for delayed and pulsed release of biologically active substances

Detailed Description Text (16):

"pH-triggering of phosphatidyl choline membrane properties via complexation with synthetic poly(carboxylic acid)s" by Seki et al in "Polym. Materials Sciences and Eng.", Proc. of Acs. Div. of Polym. Materials Meeting in Philadelphia, PA., ACS, 51, 216-219 (1984) describes the use of a synthetic poly(carboxylic acid), poly(alphaethylacrylic acid) PEAA to effect a pH-dependent release of the contents of vesicles formed from egg yolk phosphatidyl choline. Phosphatidyl choline vesicles are unaffected by PEAA at high pH but are rendered unstable at pH 7 or below. Since the pH of lysosomes is approximately 4.6, liposomes which are intact when they circulate in the bloodstream at physiological pH may be stimulated to release their contents when they are taken up by the lysosome-containing cells, usually by endocytosis.

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May 23, 1989

TITLE: Non-aqueous dental cements based on dimer and trimer acids

The base and/or filler (i.e., the powder component) may be SrO or binary mixtures of ZnO and ZrO₂, ZnO and CaSiO₃; ZnO and ethylene acrylic acid copolymer 5 (PEAA), Ca(OH)₂ and tribasic calcium phosphate; Ca(OH)₂ and MgO; Ca(OH)₂ and TiO₂, Ca(OH)₂ and ZnO, ZnO and TiO₂, Ca(OH)₂ and SrO, ZnO and SrO, or ZnO and Al₂O₃. If ZnO is used, the powder is preferably micronized. All percentages and ratios referred to herein are by weight, unless otherwise stated. Additional fillers may be included in the mixtures used.

Preferably, when a ZnO-containing powder (except when mixed with PEAA or Ca (OH).sub.2) is used, ZnO is about 20-90 weight percent of the powder, and a powder to liquid ratio of greater than 4, and preferably at least 5, up to at least 10, is used. When ZnO is mixed with PEAA in a powder, ZnO should be about 92-80 weight percent of the powder. The use of PEAA as a filler does not significantly affect the preferred powder/liquid (P/L) ratio.

TABLE B	CEMENT ADDITIVES	Formula or Name
Acronym	Form	Source
		Tribasic HA Powder
Fisher Scientific	Calcium Co.	Fairlawn, Phosphate NJ Titanium Oxide TiO_2
Powder	Fisher Scientific Co.	Fairlawn, NJ Calcium CaSiO_3 Powder Interpace Corp.
Metasilicate	Willsboro, NY Zirconia ZrO_2 Powder Applied (Zirconium Ceramics, Inc. Dioxide)	Atlanta, GA Aluminum $\text{Al}(\text{OH})_3$ Powder Matheson, Hydroxide
Coleman & Bell	Norwood, OH Aluminum Oxide Al_2O_3 Powder Alcoa Chemicals (Hydral 710)	Bauxite, AR poly(methyl PMMA Powder Esschem methacrylate)
Essington, PA	poly(vinylidene PVF ₂) Powder Penwalt Corp.	fluoride (Grade 960 ES)
Philadelphia, PA	Ethylene/Acrylic <u>PEAA</u> 15% Acrylic Scientific Acid Copolymer	
Acid Polymer Prod.	Ontario, NY	

TABLE 1															
Properties of DA/ZnO Cements 24 H. Mechanical Strength (MPa) Powder Component P/L															
Ratio	Set.	Time	Diametral	Cement	In Powder	In Liquid	w/w	Min	Compressive	Tensile				A	
ZnO.sup.1	--	7	7.5	49.4	(2.1)	.sup.2	6.5	(0.5)	.sup.2	B	ZnO.sup.3	--	7	10.0	46.4
(1.0)	5.8	(2.5)	C	ZnO.sup.1	(86%)	, MgO.sup.4	--	4	7.0	46.6	(1.0)	5.7	(0.8)	D.sup.6	
ZnO.sup.1	ZrO.sub.2	(67%)	9	9.5	46.6	(4.8)	6.2	(0.9)	E.sup.6	ZnO.sup.5	CaSiO.sub.3				
(67%)	5	3.5	22.0	(1.0)	8.2	(0.8)	F.sup.6	ZnO.sup.1	PEAA(5%)	7	9.0	45.6	(1.3)	5.7	
(0.4)	G.sup.6	ZnO.sup.1	PEAA(10%)	7	9.5	46.9	(2.2)	5.6	(0.6)						

Micronized ZnO .sup.2 Standard Deviation .sup.3 Activated with 0.5% PA .sup.4
Activated with 1.0% AA .sup.5 Activated with 2.0% PA .sup.6 Resisted fracture under
compression at crosshead speed of 1 mm/min

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L1: Entry 20 of 23

File: USPT

Jan 7, 1986

DOCUMENT-IDENTIFIER: US 4563392 A

TITLE: Coated extended chain polyolefin fiber

Detailed Description Paragraph Table (2):

TABLE 2	Conc	Temp	F.sub.	PO	SB	Run	Polymer*				
(g/L)	.degree.C.	Regime	N	kPa							
First 0.98 1580 B EAAO 60 87	Second 1.20 2000 C PE-AA 60 105	First 1.38 2270 D PE-AA 60 205	Second 1.56 2620 E EAA2 60 95	First 1.33 2340 F EAA5 60 95	First 1.42 2340 G OPE2 60 95	First 1.25 2070 H OPE2 120 95	First 1.56 2620 I OPE6 60 95	First 1.47 2400 J OPE6 120 95	First 1.38 2270	uncoated fiber	-- -- -- 0.67 1100

*The polymers used were: EEAO -- a low molecular weight ethyleneacrylic acid copolymer of acid number 120 sold by Allied Corporation as AC 5120 copolymer PEAA -- a polyethylene graft acrylic acid having 6% acrylic acid sold by Reichhold Chemical as PE452 EAA2 -- an ethyleneacrylic acid copolymer of acid number 49.2 sold by Dow Chemical as DowPE-452. EAA5 -- an ethyleneacrylic acid copolymer of acid number 52 sold by Dow Chemical as EAA455 OPE2 -- an oxidized polyethylene of acid number 28 sold by Allied Corporation as AC 392 oxidized polyethylene OPE6 -- An oxidized polyethylene of acid number 16 sold by Allied Corporation as AC .RTM. 316A oxidized polyethylene

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L5: Entry 62 of 121

File: USPT

Feb 15, 2000

DOCUMENT-IDENTIFIER: US 6024978 A

**** See image for Certificate of Correction ****

TITLE: Pharmaceutical compositions comprising cyclosporins

Brief Summary Text (104):

4.1. Polyacrylate and polyacrylate co-polymer resins, for example poly-acrylic acid and poly-acrylic acid/methacrylic acid resins such as known and commercially available under the trade name Carbopol (c.f. Fiedler, loc. cit., pp. 254-256), in particular the products Carbopol 934, 940 and 941, and Eudragit (c.f. Fiedler, loc. cit., pp. 486-487), in particular the products Eudragit E, L, S, RL and RS and, most especially, the products Eudragit E, L and S;

Current US Original Classification (1):424/450[Previous Doc](#)[Next Doc](#)[Go to Doc#](#)

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L5: Entry 75 of 121

File: USPT

Aug 10, 1999

DOCUMENT-IDENTIFIER: US 5935599 A

**** See image for Certificate of Correction ****

TITLE: Polymer-associated liposomes for drug delivery and method of manufacturing the same

Detailed Description Text (31):

The anionic polymer typically is an acrylic polymer containing a sufficient amount of acid-containing monomers, like acrylic acid, methacrylic acid, vinylsulfonic acid, or vinylphosphonic acid. The acid-containing monomer can be, but is not limited to, acrylic acid, methacrylic acid, maleic acid, fumaric acid, itaconic acid, mesaconic acid, citraconic acid, vinylsulfonic acid, vinylphosphonic acid, and similar .alpha., .beta.-unsaturated carboxylic acids and .alpha., .beta.-unsaturated dicarboxylic acids. The polymer is in a salt form when utilized to prepare a PAL.

Current US Original Classification (1):424/450

CLAIMS:

16. The method of claim 1 wherein the synthetic of (b) (ii) polymer comprises an .alpha., .beta.-unsaturated carboxylic acid selected from the group consisting of acrylic acid, methacrylic acid, maleic acid, fumaric acid, itaconic acid, mesaconic acid, citraconic acid, vinylphosphonic acid, and mixtures thereof.

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L5: Entry 104 of 121

File: USPT

Mar 12, 1996

DOCUMENT-IDENTIFIER: US 5498420 A

**** See image for Certificate of Correction ****

TITLE: Stable small particle liposome preparations, their production and use in topical cosmetic, and pharmaceutical compositions

Brief Summary Text (46):

liposome preparation, wherein the gel is selected from gels incorporating a polyacrylic acid, a gel-forming cellulose compound, or a sodium salt of an acrylic acid-acrylamide copolymerisate; such a

Brief Summary Text (70):

process, wherein in step (b) polyacrylic acid, a gel-forming cellulose compound, or a sodium salt of an acrylic acid-acrylamide copolymerisate is employed as jellifying agent; such a

Brief Summary Text (119):

Liposome preparations for topical application are usually mixed with polymer jellifying agents to increase viscosity and improve application. For this purpose, especially polyacrylic acid (0.2 to 1.5%), gel-forming cellulose derivatives (0.2 to 3%) and sodium salts of acrylic acid/acrylamide copolymerisates (CTFA nomenclature -1 to 4%); commercially available as Hostacerin PN73.RTM.) in the concentrations indicated are used. When adding such jellifying agents to liposome preparations made of pure lecithin, the vesicles frequently aggregate as a result of interactions with the polymer or otherwise. In contrast to that, the fatty acid-esterified collagen hydrolysate-containing vesicles according to the invention surprisingly show only a slight change in vesicle size after having been made into polymer gels. This is documented in the following Table 5.

Current US Original Classification (1):

424/450

CLAIMS:

10. A liposome preparation according to claim 9, wherein the gel is selected from the group consisting of a polyacrylic acid, gel a cellulose gel, or a sodium salt of an acrylic acid-acrylamide copolymerisate.

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